



## PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**In re Application of: van Esch et al.**

**Serial No.: 10/656,839**

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**For: GELLING AGENTS OR THICKENERS**

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**CERTIFICATE OF MAILING**

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## COMMUNICATION

Commissioner for Patents  
P.O. Box 1450  
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Sir:

Enclosed is a copy of Priority Document 01200836.3 filed March 6, 2001, for the above referenced application.

Respectfully submitted,

John Franklin

Andrew F. Nilles  
Registration No. 47,825  
Attorney for Applicant(s)  
TRASKBRITT, P.C.  
P.O. Box 2550  
Salt Lake City, Utah 84110-2550  
Telephone: 801-532-1922

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Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécifiée à la page suivante.

Patentanmeldung Nr. Patent application No. Demande de brevet n°

01200836.3

Der Präsident des Europäischen Patentamts;  
Im Auftrag

For the President of the European Patent Office  
Le Président de l'Office européen des brevets  
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R C van Dijk

DEN HAAG, DEN  
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Anmeldung Nr:  
Application no.: 01200836.3  
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Anmelder/Applicant(s)/Demandeur(s):

Applied NanoSystems B.V.  
Nieuwe Kerkhof 6  
9712 PT Groningen  
PAYS-BAS

Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:  
(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.  
If no title is shown please refer to the description.  
Si aucun titre n'est indiqué se referer à la description.)

Gelling agents or thickeners

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06. 03. 2001

Title: Gelling agents or thickeners

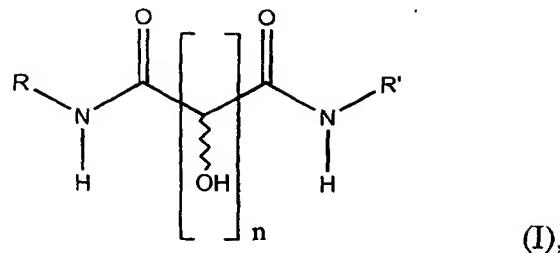
(38)

The invention relates to a novel class of gelling agents, a process for producing them and to their application in preparing gels for various applications.

Thermally reversible gelling or thickening of organic solvents by low 5 molecular weight compounds are of particular interest for hardeners of spilled fluids and cooking oils, thickeners for paints, cosmetic materials and several other technical applications. The self assembly of these gelator/thickener molecules occurs by means of non-covalent interactions such as hydrophobic interaction,  $\pi$ - $\pi$  interactions, electronic interactions, hydrogen bonding or 10 combinations thereof. Although several gelator/thickener molecules have been identified during the last decade, there is still interest in stable gelator/thickeners that can be synthesized easily from cheap, renewable sources and gelate or thicken a wide variety of solvents.

The present invention aims to provide a novel class of gelling agents 15 or thickeners. It is an object of the invention to provide gelling agents or thickeners that are based on readily available and economically attractive starting materials. It is further an object of the invention to provide gelling agents or thickeners that are capable of gelling or thickening a wide variety of solvents making the gelling agents or thickeners suitable to be employed in 20 various applications. Other objects of the invention will become clear from the discussion of the invention and a number of its embodiments presented below.

Surprisingly, it has been found that the above objects can be reached by preparing gelling agents or thickeners from low molecular carbohydrates. The present invention relates to a gelling agent in the form of a N,N'- 25 disubstituted aldaramides and N,N'-disubstituted pentaramides and derivatives thereof. Specifically, the invention relates to a gelling agent having the following structure



wherein n is 3 or 4, and wherein R and R' represent the same or different substituents chosen from the group of substituted or unsubstituted, branched, possibly aromatic groups containing, cyclic or linear alkyl, alkenyl, alkynyl groups having from 1 to 40 carbon atoms. In a preferred embodiment, R and R' each represent independently a linear, branched, or cyclic alkyl group having 4-20 carbon atoms. More preferred is that R and R' each are independently selected from the group of cycloalkyl groups having 4-16 carbon atoms. In a preferred embodiment, R and R' represent the same substituent.

5

10 It is one of the advantages of the present gelling agents or thickeners can be based on naturally occurring products, such as carbohydrates. Thus, the starting materials for producing them are from a renewable source.

15 A gelling agent or thickener according to the invention may be prepared by converting an aldose or pentose to its corresponding aldaric or pentaric acid, or a salt thereof, such as an alkali metal salt or an (alkyl)ammonium salt. It is preferred to use an aldose or pentose chosen from the group of allose, altrose, glucose, mannose, gulose, idose, galactose, talose, ribose, arabinose, xylose, lyxose and derivatives thereof, as these lead to

20 products having particularly favorable gelling and/or thickening properties. It is to be noted that both the L and the D isomers of the aldose or pentose, as well as mixtures thereof, can be used. Suitable derivatives of the mentioned aldoses and pentoses include deoxy aldoses or pentoses, ethers, esters and the like. In a more preferred embodiment, D-glucose is chosen as aldose.

25 The conversion of the aldose or pentose to its corresponding aldaric or pentaric acid is generally achieved by oxidation. The oxidation can suitably

be carried out using Pt/O<sub>2</sub>, TEMPO/NaOCl/(NaBr) or HNO<sub>3</sub>/(NaNO<sub>2</sub>) as an oxidizing agent. Further details for the manner in which the oxidation may be carried out can be found in US patents 5,831,043, 5,599,977 and 6,049,004, and in J. Org. Chem., 1977, 42, 3562-3567; J-F. Thaburet *et al.*, Carbohydr.

5 Res. 330 (2001), 21-29, all of which are incorporated herein by reference.

The thus obtained aldaric or pentaric acid or salt thereof is subsequently condensed with a primary amine to obtain the objective gelling agent or thickener.

The aldaric or pentaric acid can be condensed with an amount of at

10 least 200 mole%, with respect to the aldaric or pentaric acid, of a primary amine. It is preferred to activate the aldaric or pentaric acid first by means of lactonization and/or esterification, depending on the stereochemistry of the carbohydrate. Further details may be found in Kurtz *et al.*, J. Biol. Chem., 1939, 693-699; Hoagland, Carbohydrate Res., 1981, 98, 203-208, and US

15 patent 5,312,967, which are incorporated herein by reference.

In an alternative embodiment, non-symmetrical N,N'-dialkylaldaramides or N,N'-dialkylpentaramides may be prepared, wherein R and R' represent different substituents. In accordance with this embodiment, the aldaric or pentaric acid may be converted into an N-alkyl-1-

20 aldar/pentaramid-6-ate or N-alkyl-6-aldar/pentaramid-1-ate (as disclosed in US patent 5,239,044; L. Chen *et al.*, J. Org. Chem., 61 (1996) 5847-5851; R. Lee *et al.*, Carbohydr. Res. 64 (1978) 302-308; and K. Hashimoto *et al.*, J. Polym. Sci. Part A, Polym. Chem., 37 (1999) 303-312), activated, and subsequently condensed with, preferably 100 mole% with respect to the N-

25 alkyl aldar/pentar-ate, of a second primary amine.

In general, the obtained gelling agent or thickener precipitates from the reaction mixture in which it is formed and can be easily isolated by filtration. Further purification can be performed by conventional techniques like crystallization or, in the case of products based on galactaric acid

30 derivatives, by thoroughly washing with ethanol, water, acetone or hexane.

It will be understood that the use of the present gelling agents or thickeners to prepare a gel or to thicken a composition is also encompassed by the invention. As is well-known, gelling behavior of compounds or compositions is highly unpredictable. In principle, a solution of a specific compound in a 5 solvent, e.g. an organic solvent, is considered a gel when a homogeneous substance is obtained which exhibits essentially no gravitational flow. Preferably, the gelling phenomenon is thermoreversible. However, in as far as the present compounds do not provide a gel in a composition, they may be used as a thickener or rheology controlling agent as their addition to a composition 10 may give rise to an increase in viscosity of the composition.

Compositions in which the present compound have been found to produce a gel include compositions in numerous organic solvents. Preferred examples include aromatic and non-aromatic hydrocarbons, alcohols, ethers, esters, aldehydes, alkanoic acids, epoxides, amines, halogenated hydrocarbons, 15 silicon oils, vegetable oils, phosphoric esters, sulfoxides and mixtures thereof. In order to obtain a gel, the gelling agent or thickener is preferably mixed with the composition to be transformed to a gel in an amount of between 0.01 and 50 wt.%, based on the weight of the composition. In a preferred embodiment the mixture of the gelling agent or thickener and the composition is heated to 20 allow for an even better gel formation or thickening. Typically, the heating will involve raising the temperature of the mixture to about 30 - 175 °C until a clear solution is obtained. In an alternative embodiment, the gelling agent is first dissolved in a polar or apolar solvent and then added to or sprayed into a composition or solvent to be converted into a gel.

25 The resultant gel or thickened composition, which is also encompassed by the present invention, may find use in one of numerous applications. It is conceived that such applications lie in the field of cosmetics, oil recovery (e.g. from the sea), food products, transport of industrial solvents, stabilization of organic solvents under near zero gravity conditions, stiffening 30 of fuels to increase stability and reduce fluidity, lubricants, coatings, printing

inks, and adhesives. In these applications they may be used analogous to conventional gelling agents or thickeners, which they replace.

The invention will now be further elucidated by the following, non-restrictive examples.

5

#### Example 1a

##### Synthesis of starting materials (literature procedures)

a) Potassium hydrogen D-glucarate. - Conc. Nitric acid (258 ml, 4 moles) was heated to 50-55 °C with constant stirring (mechanical stirrer), and NaNO<sub>2</sub> (0.1 g, 1.4 mmole) was added. Glucose (180 g, 1 mole) was added in portions and the temperature was maintained at 50-60 °C by cooling with cold water. The reaction was allowed to continue for 1 h at this temperature and subsequently cooled to room temperature. 45% NaOH potassium hydride was carefully added with stirring to obtain a pH of 10-11. After cooling to room temperature, the solution was adjusted to pH = 3.4 with conc. nitric acid. The mixture was allowed to stand overnight and the precipitate was collected by filtration. The product was washed with cold 25% ethanol and dried in the air to yield potassium hydrogen D-glucarate (98.3 g, 0.42 mole, 42%).

b) D-Glucaric acid (lactone).- Potassium hydrogen D-glucarate (10.00 g, 43 mmole) was added to boiling H<sub>2</sub>O (100 ml). Active coal was added and the suspension is stirred for 0.5 h. After filtration the hot solution was added to a column of Dowex H<sup>+</sup> (4x8, 200-400 mesh) and washed with H<sub>2</sub>O (200 ml) and evaporated. Yield glucaric acid (lactone) 7.35 g.

c) D-Glucaro-6,3-lactone.- The 4.06 g crude glucaric acid (lactone) is seeded with D-glucaro-6,3-lactone (0.10 g). After 3 days the crystalline mass is triturated with acetone, the white solid collected by filtration and air-dried to yield D-glucaro-6,3-lactone (3.30 g, 17.2 mmole).

d) sodium-D-glucarate 6,3-lactone.-NaAc<sub>3</sub>.H<sub>2</sub>O (2.34 g, 17.2 mmol) was added to a solution of D-glucaro-6,3-lactone (3.30 g, 17.2 mmole) in H<sub>2</sub>O (10 ml).

White crystals began to form within 1 h. The solution was set aside for 20 h and the crystalline product was collected by filtration and washed with aceton (3 x 5 ml.). Additional product crystallized from the aqueous aceton and the crystals obtained were subsequently washed with aceton (3x5 ml).

5 The crystallization and filtration process was repeated once more and the combined white solids were air-dried to yield sodium-D-glucarate 6,3-lactone (2.68 g, 12.5 mmole, 73%).

e) Diethyl-galacterate.- A mixture of galactaric acid (Aldrich, 30 g, 143 mmole), ethanol (750 ml) and conc.  $H_2SO_4$  (6 ml) is refluxed for 24 h. The 10 pale yellow solution is filtered and cooled in the refrigerator. Yield 27.74 g (104 mmole, 73%).  $^{13}C$ -NMR ( $D_2O$ , in ppm):  $\delta$  11.73, 69.24, 68.83, 69.24, 173.23.

#### Example 1b

15 Synthesis of dicyclohexyl glucaramide. Monopotassium D-glucarate (2.50 g, 10 mmol) is added to a solution of acetyl chloride in MeOH (12.5 ml, 1.68 M) and refluxed for 3 hours. After cooling to room temperature salts were removed by filtration, and the filtrate was concentrated under reduced pressure. The syrup obtained was dissolved in MeOH (15 ml) and neutralized with triethylamine 20 until the solution became basic (pH paper. pH = 8)) and then additional triethylamine (0.5 ml) was added to the solution. Cyclohexylamine (2.47 g, 25 mmol) was added and after 4 hours stirring the precipitate was filtered off and crystallized from EtOH. The product was recrystallized from ethanol (yield 1.64 g, 4.4 mmol, 44%).

25

#### Example 2

Synthesis of dicyclododecyl glucaramide.- Monopotassium D-glucarate (2.50 g, 10 mmol) is added to a solution of acetyl chloride in MeOH (12.5 ml, 1.68 M) and refluxed for 3 hours. After cooling to room temperature salts were removed 30 by filtration, and the filtrate was concentrated under reduced pressure. The

syrup obtained was dissolved in MeOH (15 ml) and neutralized with triethylamine until the solution became basic (pH paper, pH = 8)) and then additional triethylamine (0.5 ml) was added to the solution.

5 Cyclododecylamine (4.57 g, 25 mmol) was added and after 4 hours stirring the precipitate was filtered off and crystallized from EtOH. The product was recrystallized from 2-propanol (yield 2.26 g, 4.2 mmol, 42%).

### Example 3

Synthesis of dicitronellyl glucaramide.-Citronellylamine (5.00 g, 32.4 mmole) 10 was added to a solution of D-Glucaric acid (lactone) (Example 2, 2.90 g, about 14.5 mmole) in EtOH (40 ml). After 20 h stirring the precipitate was filtered off and recrystallized from 2-propanol to yield dicitronellyl glucaramide (2.30 g, 4.75 mmole, 33%).

15 Example 4

Synthesis of didodecyl galactaramide.-Dodecylamine (3.75 g, 20.5 mmole) was added to a solution of diethyl galactarate (2.66 g, 10 mmole) in EtOH (50 ml). After 72 h stirring the precipitate was filtered and thoroughly washed with ethanol, aceton, and ether to yield didodecyl galactaramide (4.87 g, 8.9 mmole, 20 89%).

## Example 5

## Solvent scope of N,N'-dialkylaldaramides or N,N'-dialkylpentaramides

	Compound	C6GluC	C12GluC	CitGluCi	12Gal1	C6GluC1
5		6	12	t	2	2
	Cyclohexane	g.	g.	g.,c*	n.s.	-.
	Toluene	g.	g.	p.	n.s.	-.
	n-Butylacetate	g.	g.	p.	n.s.	-.
10	1,2- Dichloroethane	g/c.	g.	s.	n.s.	-.
	Ethanol	g/c.	g/c.	s.	n.s.	-.
	Dimethylsulfoxide	g/c.	g/c.	s.	g.	-.
15	water	n.s.	n.s.	c.	n.s.	-.

## Example 6

## Concentration range of N,N'-dialkylaldaramides or N,N'-dialkylpentaramides

5	Compound	C6GluC	C12GluC
		6	12
	Cyclohexane	<2.5%.	<5%.
	Methyllaurate	<2.5%.	<5%.
	Dow Corning	<2.5%.	<50%.
10	702		
	Toluene	<2.5%.	<50%.
	n-Butylacetate	<2.5%.	<50%.
	1,2-	<5.0%.	<50%.
	Dichloroethane		
15			

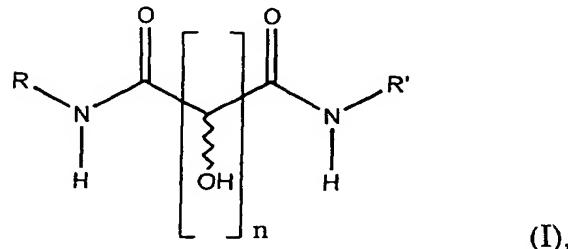
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Claims

(38)

1. A gelling agent or thickener in the form of a N,N'-disubstituted aldaramide, a N,N'-disubstituted pentaramide, or a derivative thereof.
2. A gelling agent or thickener according to claim 1 having the formula



- 5 wherein n is 3 or 4, and wherein R and R' represent the same or different substituents chosen from the group of substituted or unsubstituted, branched, possibly aromatic groups containing, cyclic or linear alkyl, alkenyl, alkynyl groups having from 1 to 40 carbon atoms.
3. A gelling agent or thickener according to claim 2, wherein R and R', 10 R and R' each represent independently a linear, branched, or cyclic alkyl group having 4-20 carbon atoms.
4. A gelling agent or thickener according to claim 3, wherein R and R' each are independently selected from the group of cycloalkyl groups having 4-16 carbon atoms.
- 15 5. A gelling agent or thickener according to any of the claims 2-4 wherein R and R' are the same.
6. A process for preparing a gelling agent or thickener according to any of the preceding claims, comprising oxidation of an aldose or pentose to form an aldaric or pentaric acid or a salt thereof, and condensation with a primary amine of the formula  $\text{RNH}_2$  and a primary amine of the formula  $\text{R}'\text{NH}_2$ .
- 20 7. A process according to claim 6, wherein the aldaric or pentaric acid or salt thereof is activated before condensation by lactonization and/or esterification.

8. A process according to any claim 6 or 7 wherein the aldose or pentose is chosen from the group of allose, altrose, glucose, mannose, gulose, idose, galactose, talose, ribose, arabinose, xylose, lyxose and derivatives thereof.
- 5 9. A process according to claim 8, wherein the derivative is a deoxy aldose or pentose, an ether, or an ester.
10. A process for preparing a gel or thickening by mixing a gelling agent or thickener according to any one of claims 1-5 with a composition.
11. A process according to claim 10 wherein the composition comprises 10 an organic solvent.
12. A process according to claim 11 wherein the solvent is chosen from the group of aromatic and non-aromatic hydrocarbons, alcohols, ethers, esters, aldehydes, alkanoic acids, epoxides, amines, halogenated hydrocarbons, silicon oils, vegetable oils, phosphoric esters, sulfoxides and mixtures thereof.
- 15 13. A process according to any one of claims 10-12 wherein the gelling agent or thickener is mixed with the composition in a ratio of between 0.01 and 50% by weight.
14. A process according to any one of claims 12-13 wherein the mixture of the gelling agent or thickener and the composition is heated, or wherein a 20 solution of the gelling agent or thickener is added to or sprayed into the composition.
15. A gel comprising a gelling agent or thickener according to any one of claims 1-5.
16. A gel according to claim 15 obtainable by a process according to any 25 one of claims 10-14.

Title: Gelling agents or thickeners

06. 03. 2001

(38)

Abstract

The invention relates to a novel class of gelling agents or thickeners, to a process for preparing said gelling agents or thickeners and to their use to prepare gels. The present gelling agents or thickeners have the form of a N,N'-disubstituted aldaramide or N,N'-disubstituted pentaramide.

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